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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/857,308

Applicant(s)

ITOH ET AL.

Examiner

Christopher H Yaen

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-5, 16, 18 and 21-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-15, 17, 19, 20, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 & 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Sequence Alignments.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the search would not be burdensome. This is not found persuasive because the inventions of the different groups are not related to one another by either structure or function. A search of the different groups would require searching in different databases, requiring a search that is not overlapping nor co-extensive. Applicant's request to rejoin claim 7 into group II is granted, as such claim 7 will be examined as part of group II.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 29 is newly added.
3. Claims 1-29 are pending in the instant case, claims 1-5, 16, 18, and 21-27 are withdrawn from further consideration. Applicant's is reminded to cancel claims drawn to non-elected inventions.
4. Therefore, claims 6-15, 17, 19-20, and 28-29 are examined on the record. Applicant's election of SEQ ID No: 5 as the species is acknowledged. As a result, all claims will be read to the extent that they read on SEQ ID No: 5.

Information Disclosure Statement

5. The Information Disclosure Statements filed 6/1/2001 and 11/4/2002 (paper no. 3 and 12) are acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Objections

6. Claims 17, 19, and 28 are objected to because of the following informalities: the claims are dependent on non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 6, and 9-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 6, and 9-15 as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 112, 1st paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9-15, 17, 19-20, and 28-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite a "partial peptide", and "derivative" or "derivatives", as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature that provides the recited function of the "partial peptide", "derivative" or "derivatives". The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice any partial peptide of a tumor antigen of SEQ ID No: 1, nor any of its derivative or derivatives. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the function of a tumor antigen of SEQ ID No: 1. The genus of

compounds encompassed by these terms is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed partial peptides and or derivatives and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. *Id.* 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 112, 1st paragraph

11. Claims 7-8, 17, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising tumor

antigen protein for treating cancer cells in vitro, does not reasonably provide enablement for a pharmaceutical composition comprising a tumor antigen protein for preventing cancer cells in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a pharmaceutical composition comprising as an active ingredient a tumor antigen protein of SEQ ID No: 1 or encoded by a nucleic acid molecule of SEQ ID No: 2.

The specification teaches that a CTL response was induced when the isolated tumor antigen protein was used to stimulate HLA containing target cells in vitro. This data indicates that the tumor antigen-HLA complex was able to trigger an immune response as measured by IFN- γ production. However, the specification has not taught one of skill how to extrapolate these findings of CTL response into methods of preventing tumors or whether this tumor antigen is effective as an in vivo pharmaceutical composition.

Reasonable guidance with respect to preventing any cancer (not just lymphomas) relies on quantitative analysis from defined populations which have been successfully prescreened and predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential elements towards the validation of a preventative therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of

disease. This irrefutable link between antecedent drug and subsequent knowledge of prevention of the disease is the essence of a valid preventative agent. Further, a preventative administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. Although the design of an effective, well tolerated, and less toxic drug for cancer prevention is in its infancy, little progress in discovering such a drug has been made (Evans et al Q.J.Med 1999;92:299-307). Evans *et al* argues that limited understanding in the use of vaccines in advanced diseases, the long-term preventative effects, and lack of clinical trials leads to the notion that cancer prevention is not yet feasible (see page 303).

The specification has only discussed the use of the instantly claimed protein in an in vitro setting and has not taught the skilled artisan how such a tumor antigen is to be administered or used in vivo as a pharmaceutical composition. One cannot extrapolate the teachings of the specification to the scope of the claims because the specification provides no exemplification of or guidance on how to use the claimed pharmaceutical composition for immunization purposes with any predictability. With regards to tumor immunotherapy, the goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. Treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either

Art Unit: 1642

cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy. As such, pharmaceutical compositions for the treatment or prevention of cancer is considered unpredictable in the absence of guidance in the form of working examples.

Therefore, given the rather unpredictable nature of the cancer prevention, the lack of information with regard to the use of cancer compositions as pharmaceuticals, and the lack of teachings to overcome the unpredictable nature of the art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 6,9, and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagase *et al* (DNA Res. 1998 Oct; 5(5):277-286). Claims are drawn to a tumor antigen protein encoded by a DNA encoding a protein comprising the amino acid of

SEQ ID No: 1, wherein the antigen is a partial peptide, wherein the antigen is has all or part of a sequence from SEQ ID No: 5, and wherein the 2nd amino acid from SEQ ID No: 5 is a tyrosine. Nagase *et al* teach the characterization of SEQ ID No: 1 and further disclosed the characterization of other sequences which are similar or identical to that of SEQ ID Nos: 1 and 5. Furthermore, Nagase *et al* teach a protein of SEQ ID No: 5 in which the second amino acid is a tyrosine. Although the reference does not specifically teach that the purified peptide are able to bind to HLA, the claims are drawn to the product *per se* and inherently, such a polypeptide would bind to the HLA. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

14. Claims 6-15, 17, 19-20, and 28-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Sette *et al* (WO 99/45954). Claims are drawn to a tumor antigen that is encoded by a DNA which hybridizes to any DNA that encodes SEQ ID No: 1 or a DNA comprising SEQ ID No: 2, and pharmaceutical composition comprising said tumor antigen as an active ingredient. The claims are further limited to a partial peptide that is derived from the said tumor antigen wherein said antigen is able to bind to HLA, more

specifically HLA-A24, wherein said partial peptide is derived from a SEQ ID No: 5 or is a derivative of SEQ ID No: 5 (substitutions at the second position by tyrosine). It is further limited to said peptide being synthesized recombinantly. And lastly, claims are limited to a diagnostic agent comprising said tumor antigen.

Sette *et al* disclose methods of selecting immunogenic peptides that are able to bind to the HLA-A24 receptor (see page 6). In the disclosure, Sette *et al* teach that such peptides would be useful as pharmaceutical compositions for use as therapeutics and as a diagnostic agent (see page 3). The peptide sequence disclosed by Sette *et al* is a 9mer that is a partial peptide match of SEQ ID No: 5 and as such would be able to hybridize to a DNA sequence encoding SEQ ID No: 1 (see page 126, peptide F111.19). It is also disclosed by Sette *et al* that substitutions to the peptide sequence can be made, wherein such substitutions are replaced with biologically and structurally similar amino acids (see page 12). Sette *et al* teach that multiple forms of making the peptides are available including recombinant production of the peptides (see page 11).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone

Art Unit: 1642

numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
July 24, 2003

2
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